

EXHIBIT E

Our Amendment 6/14/01, page 24

In re: Harrington, *et al.*
Appl. No.: 09/513,997
Page 24

"All of the traps of the VICTR series are designed such that a fusion transcript is formed with the trapped gene. For all but VICTR 1, the fusion contains cellular exons that are located 3' to the gene trap insertion. All of the flanking exons may be sequenced according to the methods described in the following section. To facilitate sequencing, specific sequences are engineered onto the ends of the selectable marker (e.g., puromycin coding region). Examples of such sequences include, but are not limited to unique sequences for priming PCR, and sequences complementary to the standard M13 forward sequencing primer. **Additionally, stop codons are added in all three reading frames to ensure that no anomalous fusion proteins are produced.** All of the unique 3' sequences are followed immediately by the synthetic 9 base pair splice donor sequence. This keeps the size of the exon comprising the selectable marker (puro gene) at a minimum to best ensure proper splicing, and positions the amplification and sequencing primers immediately adjacent to the flanking "trapped" exons to be sequenced as part of the construction of a library database."

Emphasis added. See Sands, column 10, lines 4-23.

This shows that Sands obtains expression of the endogenous gene only to obtain nucleic acid sequence information. Protein expression is neither disclosed nor suggested. In fact, Sands teaches preventing protein expression from the endogenous gene to avoid problems with marker expression that could result from the production of anomalous fusion proteins produced by fusion of a marker protein with protein from the endogenous gene. Moreover, to express the endogenous protein would defeat the purpose, which was to knock-out endogenous